Are We Asking the Right Questions? "Is My Patient at Risk for Hepatitis C?"

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Objectives:

- Address the question of whether screening for hepatitis C meets screening criteria validity measures
- Address the complexities of risk for hepatitis C both causal and associated
- Distinguish the different hepatitis C natural histories for the abnormal and normal ALT patient
- To offer ideas on history taking that may allow identification of a greater percentage of the hepatitis C population

Case 1

A 53 year old Veteran who served in Southeast Asia is seen in clinic for f/u of diabetes. He has no current complaints. Heavy etoh till age 40, then occasional use.

PMH DM—Never on insulin
PTSD—Never hospitalized
HTN

Meds Glucophage
Hctz

Case 1 continued

PE Normal vitals
Mild truncal obesity
Increased expiratory breath sounds

Labs glucose 187
LFTs AST 74 ULN 70
ALT 57 ULN 70

In 2001 AST/ALT 67/74

In 2002 AST/ALT 57/61

Case 2

A 46 year old woman is seen for management of her hypertension

- Denies illicit recreational drug use ever
- Transfusion in mid 1990s following MVA trauma
- ALT 49 (ULN 55)

Case 3

A 69 year old man seen for post MI risk reduction

- Denies illicit drug use or blood transfusion history. Heavy alcohol use in 20s
- ALT 40 (ULN 55)
- Platelet 147 (LLN 170)

Hepatitis C Viral Reservoirs

- Liver
- Blood
- Lymph node/immunocyte
- Transmission requires contact
- Is “Have you had parenteral exposure to the blood of a person infected with hepatitis C?” the right question?

Screening

- Application of a diagnostic test in an asymptomatic population to detect disease at stage where intervention improves outcome
- Potential adverse effects from both false positive e.g., anxiety and false negatives
- Strict standards of evidence-based medicine challenges benefits of screening

Screening Strategies

- Population screening: application of test to an entire defined population e.g., mammography to women over 50 years
- Targeted screening: screening patients at high risk for a disease and already are patients in a disease register
- Case finding: looking for additional diseases in patients complaining of other problems

Case Finding Strategies

- Apply screening test to individual with risk factors for a disease
- Relatively simple and inexpensive
- May miss important populations that don’t present for care
- Relies on a primary care network

Primary Care Diagnoses
Almost all Hepatitis C

Criteria Needed for Screening Program

- Disease must be common
- Target population must be identifiable
- Screening test needs good sensitivity/specificity
- Need recall procedures
- Test needs to be accepted by population screened
- Need effective therapy

Hepatitis C and Screening Suitability

- Causes significant morbidity and is common
- High risk groups are identifiable
- Screening test (HCV antibody) is good
- There is an effective therapy—we think

Hepatitis C: A Global Health Problem

170-200 Million (M) Carriers Worldwide

World Health Organization. Weekly epidemiological record. 1999;74:421-428

Hepatitis C Virus Infection: United States

New infections (cases)/year 1985-1989 1997	 242,000 38,250
Deaths from acute liver failure	Rare
Persons ever infected (1.8%)	3.9 million (3.1 - 4.8)*
Persons with CHC	2.7 million (2.4 - 3.0)*
HCV-related chronic liver disease	40% to 60%
Deaths from chronic disease/year	8000 – 10,000
Liver transplants** Number Cost/transplant	 ~4698/year ~$300 million

*95% Confidence Interval
**UNOS, 1999
Source: CDC/Hepatitis Branch

Excludes many high risk groups

HCV Antibody Identifies Viral Exposure

- Specificity and sensitivity both around 99%
- Rare instances of false negative causes in acute infection and severe immune compromise
- Current generation EIA become positive within 8 weeks or less of exposure
- Antibody is first investigation in screening
- False $^{+}$ rare, easily clarified with PCR hep C

Treatment: Interferon and Ribavirin

- Eliminates virus in about half the cases
- Evidence-based medicine arguments have not always found evidence that screening and treatment decreases mortality
- U.S. Preventative Services Task Force has used these arguments to dismiss hepatitis C as a potential candidate for screening
- Other experts have countered that failure to show mortality benefit is due to long duration of the disease
- Viral eradication and ALT normalization should/could be a surrogate for decreased mortality

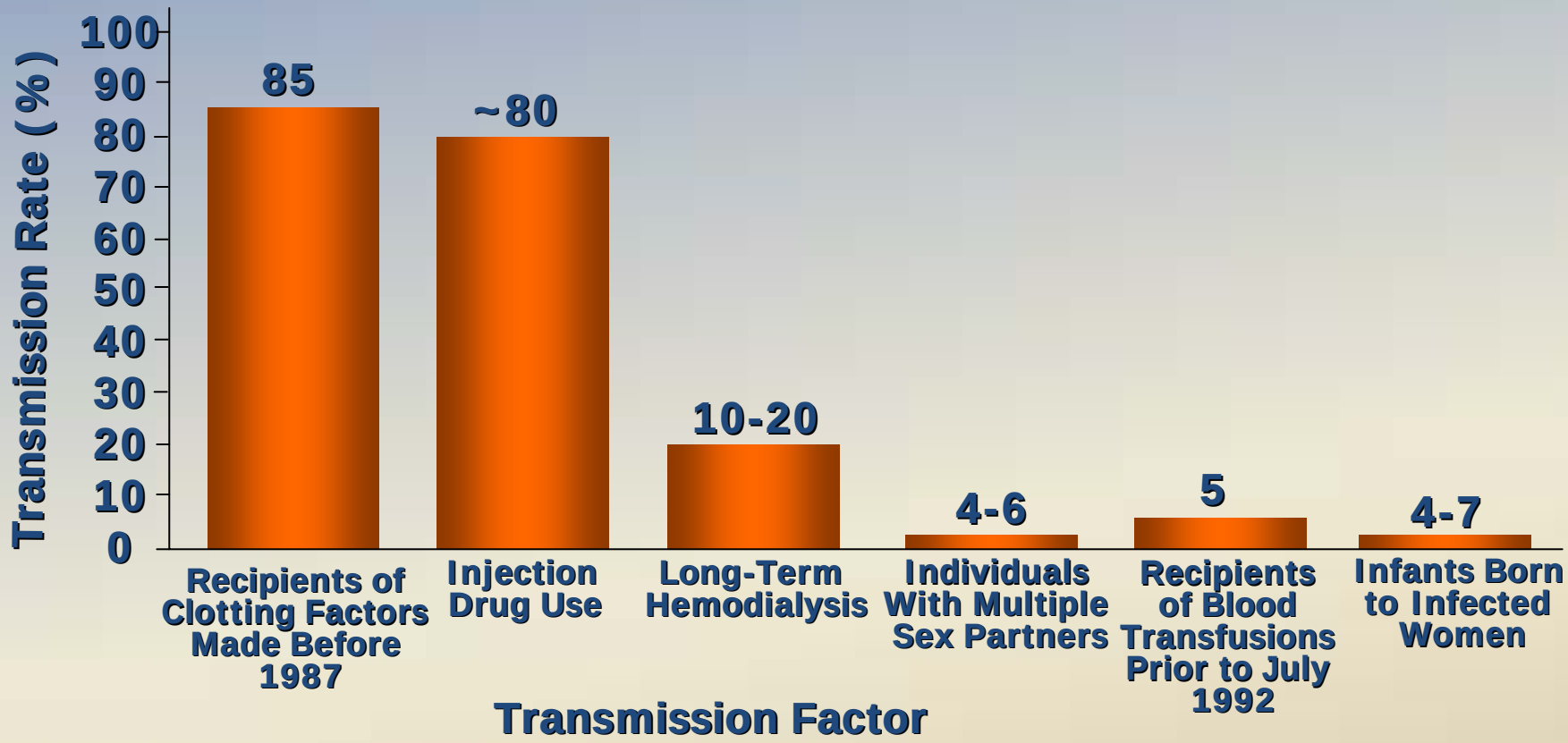
Screening Endorsements by Different Societies

- Endorsed by multiple national/international societies
- Recommend selective screening in targeted groups
- No population screening (VA exception?)
- Low prevalence HCV inside identifiable risk groups
- Half of these undetected patients have slowly progressive disease
- Have contradicting conditions
- QOL deterioration from knowing result
- Mass screenings not cost effective

Guidelines for HCV Risk Factors for Which There is Consensus

- There are major risk factors: screen these
- Any injection drug use ever
- Blood transfusion/other exposure to unscreened blood
- Abnormal ALT

Hepatitis C Virus
High Risk Profile



Alter et al. *N Engl J Med*. 1999;341:556-562.
NIH Consensus Development Conference Statement. 2002.
Ohto et al. *N Engl J Med*. 1994:330:744-750.

Lack of Consensus on Minor Risk Factors

- VA has examined HCV prevalence in a large data base

Veterans—Prevalence

- 6.6% of VAH population vs 1.8% civilian population nationwide
- San Francisco: 17.7% of VA population
- Risk factors seem to be related to traditional risk factors rather than combat risk factors
- Average age 48; 60% between 41 and 50
- Active duty personnel: recruits .1% vs 3% over age 40
- HCV infection in VA patients reflects service in Vietnam era

Table 1. Potential risk factors for hepatitis C virus (HCV) infection in 1,032 veterans tested for the disease[6]

Factor	% of patients reporting factor	
	HCV negative	HCV positive
Sex with a prostitute	54	68
Sexually transmitted disease	38	54
> 15 opposite sex partners	41	62
> 15 same sex partners	10	10
Transfusion	30	30
Transfusion before 1992	19	24
Needle stick	10	20
Acupuncture	22	30
Tattoo	20	50
Body piercing	24	37
Injectable drug use	5	61
Needle sharing	61*	77*
Cocaine use	23	72
Straw sharing	85†	83†
Crack cocaine use	42†	65†
Drug or alcohol abuse treatment	19	59
Incarceration	21	64

*Percentage of patients calculated among those reporting injectable drug use. †Percentage of patients calculated among those reporting cocaine use.

--Cheung

Table 3. Veterans Affairs screening guidelines for hepatitis C testing

Vietnam-era veteran
Blood transfusion before 1992
Past or present intravenous drug use
Unequivocal blood exposure of skin or mucous membranes
History of multiple sexual partners (> 10 lifetime sexual partners)
History of hemodialysis
Tattoo or repeated body piercing
History of intranasal cocaine use
Unexplained liver disease
Unexplained abnormal alanine aminotransferase
Heavy use of alcohol (50 g or more of alcohol per day for ≥ 10 y)
Patient wants to be tested

Prevalence of HCV in U.S. Prisons

- 12 to 31%
- Incarceration may be a surrogate for injection drug use
- Non regulated tattoo application may be independent risk for acquisition

Risk Factors Accepted by All Guidelines

- Intravenous drug use ever
- Blood transfusion or transplant before 1992
- Receipt of clotting factors before 1987
- Clinical or biochemical evidence of chronic liver disease
- Needle sticks or other percutaneous exposures
- Hemophilia
- Children of HCV^{+} mothers
- HIV
- Sexual partners of HCV^{+} patients

Risk Factors for Which Testing is Indicated by some guidelines

- Population with high prevalence e.g., Veterans, high risk countries
- Incarceration—past vs present
- Hepatitis B
- Sharing intranasal cocaine equipment
- History of STD with genital erosions
- Traumatic sex or sex during menstruation
- Health care workers performing invasive procedures

Risk Factors for Which Testing Usually Not Formally Recommended

- Injections (medical) with reusable glass syringes
- Heavy marijuana use
- Sexual promiscuity
- Poverty
- History of invasive procedures
- History of surgery
- Cosmetic treatments

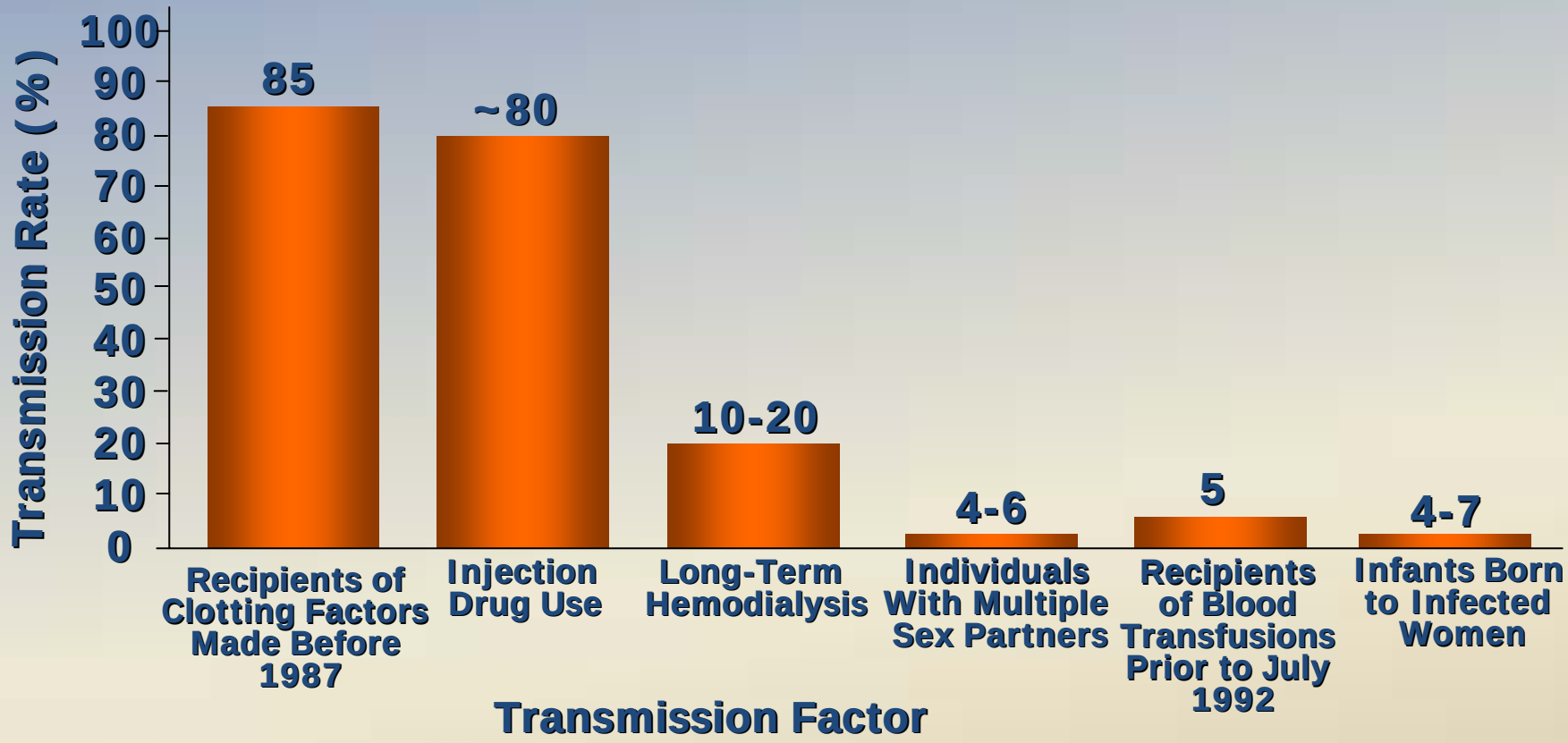
Stigma Associated with Risk Factors

- Personal psychological, social, economic, legal concerns
- Concealment is common
- Patients may have easier time acknowledging a surrogate risk factor
- Offering the patient a bland, generic out such as “Have you had any contact with another person’s blood that you think might have put you at risk for hepatitis C?” may be a useful strategy

Persistently Normal ALT Patient

- Normal ALT patients less likely to progress to cirrhosis than elevated ALT patients
- 14-24% of normal ALT patients will have more than portal fibrosis on liver biopsy (including cirrhosis)
- About 75% of abnormal ALT patients will have grater than portal fibrosis on liver biopsy
- Significant risk for a portion of the normal ALT patients to progress

Hepatitis C Virus
High Risk Profile



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HCV: Risk factors for infection

Testing (3)

- Vietnam-era service[1]
- Blood transfusion before 1992
- Past or present intravenous drug use
- Unequivocal blood exposure of skin or mucous membrane
- History of multiple sexual partners[2]
- History of or current hemodialysis
- Tattooing or repeated body piercing
- History of intranasal cocaine use
- Unexplained liver disease
- Unexplained abnormal ALT
- Heavy use of alcohol[3]

1. Dates of service between 1961-1975
2. Defined as more than 10 lifetime sexual partners
3. Defined as more than 50 grams of alcohol per day for 10 or more years (an average drink contains 10-12 grams of alcohol)

How Do We Do On Screening?

- Surveys of practitioners reveal wide variation in risk factor knowledge and screening practices
- A study of 229 hep C patients from 26 clinics in Michigan showed 20% were identified from physician-identified risk factors—rest ALT elevation or patient request
- Only 10% asked about risk factors during their first clinic visit

Summary

- Screen ALT
- Screen major causal risk factors
- Consider directed screening of minor causal risk factors
- Consider that a risk factor may be unacknowledged and that a pattern of risky behaviors unrelated to hepatitis C transmission may direct a screen for the virus
- Screening has the potential for significant health benefits